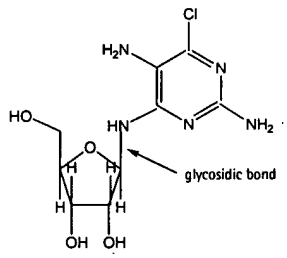
REMARKS

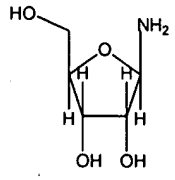
In an Office Action mailed September 13, 19999, claims 9, 18 – 22 are pending and all claims stand rejected. Claims 9, 18, and 22 have been amended for clarification. Claims 9 and 18 - 22 are pending.

Claims 9, and 18 - 22 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In response to the Examiner's specific points:

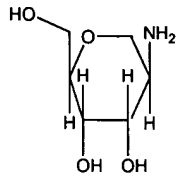
1. An example of a glycosidic bond is the bond between the aglycone and the glycoside in a nucleoside. A glycosidic bond is indicated for the following example:



R^3 cannot be, for example, a group that would be attached by a glycosidic bond such as the precursor to a riboside (1-aminoribose) shown below



because it is not stable under the conditions required for condensation with dichloropyrimidines. In contrast, cylopentylamine is stable. Therefore, R^3 groups, such as an amine in which the carbon substituted by the nitrogen is also substituted by an oxygen are not stable; whereas, if the oxygen is moved over one position relative to the amine, then the amine is stable (no longer a glycosidic bond).



2. Claims 9 and 18 – 22 have been amended to clarify the Examiner's point regarding heteroatoms. Support for the amendment is found in the specification at page 10.

4. The term "group" has an ordinary dictionary definition.

Claims 9 and 18 have been amended for clarification in that " C_{2-8} hydrocarbyl " now replaces "acyclic". Support for the amendment is found in the specification at pages 10 – 11. The claim language is now as in the claims originally filed.

Applicants believe that claims 9 and 18-22 as amended overcome the rejection under 35 U.S.C. §112. Applicants respectfully request withdrawal of the rejection of claims 9 and 18-22 under 35 U.S.C. §112.

Claims 9, and 18-22 are rejected under 35 U.S.C. §103 as being unpatentable over U.S. Patent No. 5,087,697 (Daluge) in view of U.S. Patent No. 4,916,224 (Vince) or U.S. Patent No. 5,049,671 (Daluge) further in view of Norbeck, Vince, Borthwick or Shealy. The Examiner states that " Applicants make a lot of assertions without presenting evidence." Applicants respectfully disagree. The evidence is in the art of record. Example 1 of the Shealy process reference describes a product that is a "dark red syrup" and which is obtained in low yield. Example 15 of the Borthwick reference describes products that are "sticky foams" and "red filtrates", intermediates that are unsuitable for large scale manufacture of product. Triaminopyrimidine

intermediates such as 6b of the '224 reference are air- and light- sensitive and extremely difficult to purify due to their polarity and metal-chelating abilities (specification at page 13). Disadvantages of the '607 process are purification by column chromatography (e.g. Example 5) and/or low yield (e.g. Example 6).

The substituent at the two position of the pyrimidine ring of the '697 compounds, designated NR^3, represents an amino group bearing a protecting group. **Protection of the amino group was thought necessary at the time because inefficient chlorination of 2,5-diamino-4,6-dihydroxypyrimidine was reported. Such chlorinations resulted in extensive degradation of the starting pyrimidine to copious tars. (Legraverend, M. et al, Synthesis, 1990, 587-589; previously cited).**

In contrast to the processes and intermediates of the references cited the claimed process results in a white powder at high yield, with no contaminants (see Example 8). Processes prior to the present invention, for example the '697 process, used intermediates that were protected at the 2 position **because a way of making the de-protected compounds without resulting tars or hydrolysis was not known.** Therefore, nothing in '697, '224, '671, Norbeck, Borthwick, or Shealy would motivate the person of ordinary skill in the art to use the intermediates of formula VI in the claimed process.

The '697 reference does not teach the removal of the protecting group until after ring closure to form the purine, because deprotection before ring closure causes the compound to fall apart. The secondary references describe processes that are fraught with problems of mixtures, contaminants and poor yield. In order for a §103 rejection to be proper, the combined references must suggest the claimed modification or motivate the person of ordinary skill in the art to make the modification. The '697 reference in view of the secondary references clearly does not suggest the claimed modification because, as discussed above, it would not occur to one skilled in the art that such a modification could be made with success. To make these modifications, the person of ordinary skill in the art would have to use hindsight from reading the present specification, and hence, the person of ordinary skill in the art would only have an invitation to experiment from the disclosure of '697, '224, '671, Norbeck, Borthwick, and Shealy.

Applicants respectfully point out that, as is well known, hindsight is impermissible and an invitation to experiment is not the test for obviousness. Rather, the reference must teach the claimed invention as a whole, including the desirability of compounds of formula VI in the claimed process to make products in high yield and purity. Therefore, Applicants respectfully submit that the rejection under §103 is improper and should be withdrawn.

Claims 9 and 18 – 20 are rejected under 35 U.S.C. §103 as being unpatentable over EP 413544 in view of Norbeck, Vince, Borthwick or Shealy. The compounds of EP413 544 are outside the scope of the present application because $O(CH_2)_3OR_5$ does not fall within the definition of R^3. The EP 413544 process results in complex mixtures, decomposition, the necessity for harsh conditions, and low yields (see Example 1 of EP413544). Norbeck, Vince, Borthwick and Shealy are discussed above. **In contrast to the EP 413544 process and those processes and intermediates described in the secondary references, the claimed process results in a white powder at high yield, with no contaminants (see Example 8).** EP 413544 does not teach the use of acid together with orthoformate and since the process results in complex mixtures, decomposition and low yields, it is unsuitable for large-scale manufacture and formulation. The secondary references do not suggest the benefits of using the intermediates of Formula VI in the claimed process. In order for a §103 rejection to be proper, the combined references must suggest the claimed modification or motivate the person of ordinary skill in the art to make the modification. EP 413544 in view of the secondary references clearly does not suggest the claimed modification because, as discussed above, it would not occur to one skilled in the art that such a modification could be made with success. To make these modifications, the person of ordinary skill in the art would have to use hindsight from reading the present specification, and hence, the person of ordinary skill in the art would only have an invitation to experiment from the disclosure of EP413544, Norbeck, Vince, Borthwick and Shealy. Applicants respectfully point out that, as is well known, hindsight is impermissible and an invitation to experiment is not the test for obviousness. Rather, the reference must teach the claimed invention as a whole,

including the desirability of compounds of formula VI in the claimed process to make products in high yield and purity. Therefore, Applicants respectfully submit that the rejection under §103 is improper and should be withdrawn.

Claims 9, 18-22 are rejected under 35 U.S.C. §103 as being unpatentable over Norbeck, Vince, Borthwick or Shealy in view of EP 413544 or Daluge '697. The references describe processes using intermediates in which either the 2-position and 5-position of the pyrimidine ring are unprotected (Norbeck, Vince, Borthwick , Shealy), with resulting difficulties as described above or in which the 2-position and 5-position are protected (Daluge), with resulting difficulties as described above. The compounds of EP413544 are, as discussed above, outside the scope of the present invention, and furthermore, involve a synthetic route which leads to difficulties as described above. In order for a §103 rejection to be proper, the combined teachings must suggest the benefits of making the claimed modification or motivate the person of ordinary skill in the art to make the modification. Norbeck, Vince, Borthwick and Shealy in view of EP 413544 or '697 clearly do not suggest the claimed modification because, as discussed above, it would not occur to one skilled in the art that such a modification could be made with success. To make these modifications, the person of ordinary skill in the art would have to use hindsight from reading the present specification, and hence, the person of ordinary skill in the art would only have an invitation to experiment from the disclosure of Norbeck, Vince, Borthwick, Shealy, EP413544 and '697. Applicants respectfully point out that, as is well known, hindsight is impermissible and an invitation to experiment is not the test for obviousness. Rather, the references must teach the claimed invention as a whole, including the desirability of compounds of formula VI in the claimed process to make products in high yield and purity. Therefore, Applicants respectfully submit that the rejection under §103 is improper and should be withdrawn.

In view of the amendments and the foregoing discussion, it is respectfully submitted that the present application is in condition for allowance. An early consideration and notice of allowance are earnestly solicited.

Respectfully submitted,

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